REMARKS

Claims 13 and 15-20 are pending in the application. Claim 13 has been amended to be drawn to method of "lowering elevated or maintaining lowered serum parathyroid hormone levels in the human suffering from" secondary hyperparathyroidism by administering a vitamin D analog by an administration route selected from the group consisting of "a route selected from the group consisting of subcutaneous injection, intramuscular injection, intravenous injection, nasopharyngeal absorption, mucosal absorption and transdermal absorption" Support for this amendment is found in original claim 7, col. 3, line 41-60, and col. 6, lines 40-46. Applicants respectfully submit that no new matter has been added.

Claims 13 and 15-20 stand variously rejected as follows. Claims 13 and 15-20 stand rejected as being based upon a defective reissue oath/declaration under 35 USC § 251. Claims 13 and 15-20 stand rejected under 35 USC § 112, first paragraph as containing subject matter not described in the specification. Claims 13 and 15-20 stand rejected under 35 USC § 103(a) as being unpatentable over U.S. Patent No. 4,225,596 issued to DeLuca (hereinafter "DeLuca") in view of Sakhaee et al., "Postmenopausal osteoporosis as a manifestation of renal hypercalciuria with secondary hyperparathyroidism", Journal of clinical endocrinology and metabolism, Aug. 1985, 61 (2) 368-73 (hereinafter "Sakhaee"). These rejections are traversed for at least the following reasons.

Rejections under 35 USC § 251

Claims 13 and 15-20 stand rejected as being based upon a defective reissue oath/declaration under 35 USC § 251. The Examiner has asserted that the Applicants have failed to "specifically" identify at least one error which is relied upon to support the reissue application. Applicants respectfully submit that the declaration submitted January 28, 2004 adequately identifies an error which supports the reissue application as required under 35 USC § 251 and 37 CFR 1.175.

35 USC § 251 states in part that:

> "Whenever any patent is, through error without any deceptive intention, deemed wholly or partly inoperative or invalid, by reason of a defective specification or

> drawing, or by reason of the patentee claiming more or less than he had a right to claim in the patent, the Director shall, on the surrender of such patent and the payment of the fee required by law, reissue the patent for the invention disclosed in the original patent.." Emphasis added.
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> 37 CFR § 1.175 requires that:
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> "(a) The reissue oath or declaration in addition to complying with the requirements of Sec. 1.63, must also state that:
>
> (1) the applicant believes the original patent to be wholly or partly inoperative or invalid by reason of a defective specification or drawing, or by reason of the patentee claiming more or less than the patentee had the right to claim in the patent, stating at least one error being relied upon as the basis for reissue; and
>
> (2) all errors being corrected in the reissue application up to the time of filing of the oath or declaration under this paragraph arose without any deceptive intention on the part of the applicant." Emphasis added.

In order to satisfy the requirements of 35 USC § 251 and 37 CFR § 1.175, Applicants submitted a Declaration on January 28, 2004 stating the error was that the patentee claimed more than they had a right to claim in claim 1 of the application under 35 USC § 112, first paragraph. The relevant portion of the Declaration recites:

> "..this application for reissue is based on at least the error that the full breadth of claim 1 is not supported in accord with the written description requirement of 35 USC § 112, first paragraph, by the specification of the patent as filed."

The Examiner has asserted this statement is insufficient as the Examiner does not consider the statement to "specifically" identify at least one error. The Examiner does not state, nor could Applicants find, any requirement for a level of specificity with respect to the statement of error in either 35 USC § 251 nor 37 CFR § 1.175 other than the requirement to state the error. Both 35 USC § 251 and 37 CFR § 1.175 only require that a proper error be identified by the applicant. In fact, the requirement for greater specificity with respect to the error was explicitly removed from 37 CFR § 1.175. Until October of 1997, 37 CFR § 1.175(a)(1)-(6) recited that:

> "(a) Applicants for reissue, in addition to complying with the requirements of §1.63, must also file with their application a statement under oath or declaration as follows:
>
> (1) When the applicant verily believes the original patent to be wholly or partially inoperative or invalid, state such belief and reasons why.

(2) When it is claimed that such patent is so inoperative or invalid "by reason of a defective specification or drawing," particularly specifying such defects.

(3) When it is claimed that such patent is inoperative or invalid "by reason of the patentee claiming more or less than he had the right to claim in the patent," distinctly specifying the excess or insufficiency in the claims.

(4) [Reserved]

(5) Particularly specifying the errors relied upon, and how they arose or occurred.

(6) Stating that said errors arose "without any deceptive intention" on the part of the applicant." Emphasis added.

These provisions no longer exist in 37 CFR § 1.175 and were explicitly removed in the revisions to title 37 of the Code of Federal Regulations in the "Changes to Patent Practice and Procedure" finalized October 10, 1997. See 62 FR 53132, 53196. Applicants respectfully submit the Examiner cannot in effect "add" requirements back into 37 CFR § 1.175 which were specifically removed.

Applicants respectfully submit that the Declaration meets the requirements set forth in 35 USC § 251 and 37 CFR § 1.175 as the relevant statement in the submitted Declaration states that the error was that the patentee claimed more than they had a right to claim in claim 1 of the application under 35 USC § 112, first paragraph.

Rejections under 35 USC § 112, first paragraph

Claims 13 and 15-20 stand rejected under 35 USC § 112, first paragraph as containing subject matter not described in the specification. The Examiner asserts that the term "non-oral" found in claim 13, upon which claims 15-20 depend, is not supported by the specification and is considered new matter. Applicants have amended claim 13 to remove the term "non-oral" and replaced it with the language that indicates that the vitamin D analog is administered "by a route selected from the group consisting of subcutaneous injection, intramuscular injection, intravenous injection, nasopharyngeal absorption, mucosal absorption and transdermal absorption." See claim 13 as amended herein. Applicants respectfully submit that this amendment is supported by the specification. Applicants specifically point to col. 6, lines 40-46 and original claim 7 of the application. Withdrawal of the rejection is respectfully requested.

Rejections under 35 USC § 103(a)

Claims 13 and 15-20 stand rejected under 35 USC § 103(a) as being obvious over DeLuca in view of Sakhaee. The Manual of Patent Examining Procedure ("MPEP") sets forth that:

> "To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure." See MPEP § 2143.

Applicants respectfully submit that the Office Action has failed to set forth a *prima facie* case of obviousness as all the requirements for a *prima facie* case have not been met, i.e., there is no motivation or suggestion to modify or combine the references with reasonable expectation of success and the references fail to teach or suggest all the claim limitations.

No motivation or suggestion to modify or combine the references

There is no suggestion or motivation to combine or modify either the DeLuca or the Sakahaee references.

Claim 13 as amended herein, on which claims 15-20 depend, recites:

> "13. A method for lowering elevated or maintaining lowered serum parathyroid hormone levels in the human suffering from hyperparathyroidism secondary to end stage renal disease, comprising administering by a route selected from the group consisting of subcutaneous injection, intramuscular injection, intravenous injection, nasopharyngeal absorption, mucosal absorption and transdermal absorption, to a human a vitamin D analog selected from the group consisting of 1α–OH-vitamin D_2, 1α–OH-vitamin D_4, and 1α,24(R)–$(OH)_2$-vitamin D_4, wherein the analog is administered to the human in an amount sufficient to lower elevated or maintain lowered serum parathyroid hormone levels in the human." See claim 13, emphasis added.

The DeLuca patent teaches no more than the use of vitamin D analogs to treat metabolic bone disease by affecting calcium metabolism to increase absorption and retention of calcium in

the human body or for the use of regulating serum parathyroid hormone. In contrast, Applicants claimed invention, as recited in claim 13, as amended, is directed towards lowering elevated or maintaining lowered "serum parathyroid hormone levels." The DeLuca patent contains no suggestion of the use of any vitamin D analog for the treatment of secondary hyperparathyroidism. Neither the reference, nor the skill of one of ordinary skill in the art at the time the invention was made would have any motivation to modify or combine the DeLuca reference with the Sakahaee reference to provide a method for "lowering elevated or maintaining lowered serum parathyroid hormone levels in the human suffering from hyperparathyroidism secondary to end stage renal disease." The deficiencies of the DeLuca reference are not met by the Sakahaee reference.

The Sakahaee reference is directed towards postmenopausal osteoporosis as a manifestation of renal hypercalciuria with secondary hyperparathyroidism. While the Sakahaee reference discloses that postmenopausal osteoporosis may sometimes occur with secondary hyperparathyroidism, the reference does not suggest any vitamin D therapy that would treat the secondary hyperparathyroidism by regulating serum parathyroid hormone. Neither the reference itself, nor the skill of one of ordinary skill in the art at the time the invention was made would have any motivation to modify the Sakahaee reference to obtain a method of lowering elevated or maintaining lowered serum parathyroid hormone levels in the human suffering from secondary hyperparathyroidism. Furthermore, the reference provides no suggestion that would have motivated one of skill in the art at the time the invention was made to combine with the DeLuca reference to obtain a method of lowering elevated or maintaining lowered serum parathyroid hormone levels in the human suffering from secondary hyperparathyroidism.

Applicants respectfully submit that none of the cited references contain any teaching or suggestion to one of ordinary skill in the art, at the time the invention was made, that they could or should be combined or modified to provide a method of lowering elevated or maintaining lowered serum parathyroid hormone levels in the human suffering from secondary hyperparathyroidism as set forth in claim 13. As there is no motivation to combine or modify the references, Applicants respectfully submit that a *prima facie* case of obviousness has not been made.

No reasonable expectation of success

Moreover, the hypothesized combination of DeLuca and Sakahaee would not have provided any reasonable expectation of success to achieve the results of applicants' claimed invention. Claim 13 as amended herein, upon which claims 15-20 depend, is drawn to a method of lowering elevated or maintaining lowered serum parathyroid hormone levels in the human suffering from secondary hyperparathyroidism by administering by certain routes, analogs of vitamin D.

As discussed above, the DeLuca reference is directed towards the use of vitamin D analogs to increase absorption and retention of calcium in the human body or for the use of regulating serum parathyroid hormone. The DeLuca reference contains no teaching or suggestion of the use of any vitamin D analog for the treatment of secondary hyperparathyroidism. The Sakahaee reference teaches the recognition that postmenopausal osteoporosis may sometimes occur with secondary hyperparathyroidism. The reference does not contain any teaching or suggestion that any vitamin D therapy that would treat the secondary hyperparathyroidism by regulating serum parathyroid hormone levels, as recited, e.g., in claim 13. Even if the DeLuca reference and the Sakahaee reference were somehow combined, there would be no reasonable expectation that their combined teachings would serve as a method of regulating serum parathyroid hormone levels because they contain no teaching or suggestion regarding the use of vitamin D to regulate serum parathyroid hormone levels. Applicants respectfully submit that one of ordinary skill in the art at the time the invention was made would not have any reasonable expectation of success in using 1α–OH-vitamin D_2, 1α–OH-vitamin D_4, or 1α,24(R)–$(OH)_2$-vitamin D_4 to lower elevated or maintain lowered serum parathyroid hormone levels in the human suffering from secondary hyperparathyroidism.

References fail to teach or suggest all of the claim limitations

Furthermore, if it were assumed that references could somehow be combined, the combination fails to teach or suggest all of the limitations of the presently claimed invention. As discussed above, claim 13 amended herein, upon which claims 15-20 depend, contains the limitations of administering 1α–OH-vitamin D_2, 1α–OH-vitamin D_4, and 1α,24(R)–$(OH)_2$-

vitamin D_4 via certain routes to lower elevated or maintain lowered serum parathyroid hormone levels in the human suffering from hyperparathyroidism secondary to end stage renal disease.

All of the pending claims contain the limitation of administering certain vitamin D analogs to lower elevated or maintain lowered serum parathyroid hormone levels. Nether the DeLuca nor the Sakahaee reference teaches or suggests such a limitation. As pointed out earlier, the DeLuca reference teaches the use of vitamin D analogs affect calcium metabolism, to increase calcium absorption by the human body. The DeLuca reference contains no teaching or suggestion as to the use of any vitamin D analogs to regulate levels of serum parathyroid hormone in a human. The Sakahaee reference teaches the recognition that postmenopausal osteoporosis may sometimes occur with secondary hyperparathyroidism. While Sakahaee contains the teaching that dosing with hydrochlorothiazide decreases serum parathyroid hormone levels, it contains no teaching or suggestion as to the use of any vitamin D analog.

As none of the cited prior art references, alone or in combination, teach or suggest all of the limitations of claims 13 and 15-20, Applicants respectfully submit that a *prima facie* case of obviousness has not been made.

SUMMARY

Based on the foregoing, Applicants respectfully request reconsideration and withdrawal of the outstanding rejections. Applicants respectfully submit that the present application is in condition for allowance, and a favorable action thereon is respectfully requested. Should the Examiner feel that any other point requires consideration or that the form of the claims can be improved, the Examiner is invited to contact the undersigned at the telephone number listed below.

Respectfully submitted,

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